



US005854280A

United States Patent [19]
Gomez et al.

[11] **Patent Number:** **5,854,280**
 [45] **Date of Patent:** **Dec. 29, 1998**

[54] **ANTIFUNGAL SORDARIDIN DERIVATIVES**

[75] **Inventors:** Jose R. Ruiz Gomez; Jose Maria Bueno Calderon; Silvestre Garcia-Ochoa Dorado; Maria T. Fraile Gabaldon; Julia C. Pichel; Jose M. Flandor Roman; Domingo Gargallo Viola; Juan C. Cuevas Zurita; Jose L. Lavandera Diaz; Sophie Huss, all of Madrid, Spain

[73] **Assignee:** Glaxo Wellcome S.A., Spain

[21] **Appl. No.:** 669,441

[22] **PCT Filed:** Nov. 6, 1995

[86] **PCT No.:** PCT/EP95/04331

§ 371 Date: Oct. 18, 1996

§ 102(e) Date: Oct. 18, 1996

[87] **PCT Pub. No.:** WO96/14326

PCT Pub. Date: May 17, 1996

[30] **Foreign Application Priority Data**

Nov. 8, 1994 [EP] European Pat. Off. 94500173
 Nov. 8, 1994 [EP] European Pat. Off. 94500175

[51] **Int. Cl.⁶** **A61K 31/35**

[52] **U.S. Cl.** **514/456; 514/457; 514/460;**
 549/362; 549/416

[58] **Field of Search** 549/362, 416;
 514/456, 457, 460

[56] **References Cited**

PUBLICATIONS

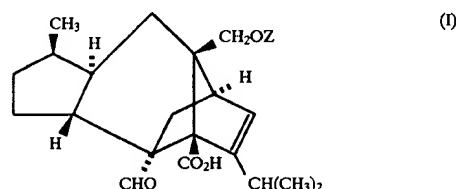
Patent Abstracts of Japan vol. 18, No. 485 (C-1248), 1994
 JPA,06 157582 Banyu Pharmadeut Co. Ltd. Jun. 1994.
 Patent Abstracts of Japan vol. 11, No. 119 (C-436), 1987
 JPA,62 040292 Sankyo Co Ltd. Feb. 1987.

Helvetica Chimica Acta, vol. 54, No. 119, Basel, CH pp. 1178-1190, XP002000182 Hauser D. and Sigg H.P.: "Isomerisierung und Abbau von Sordarin" (1971).

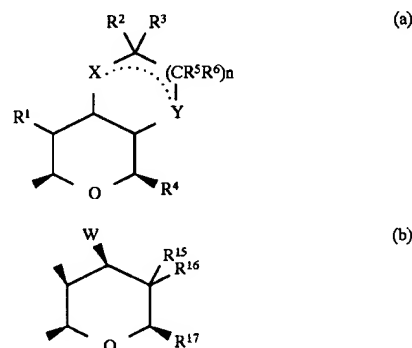
Primary Examiner—Amelia Averill Owens
Attorney, Agent, or Firm—Nixon & Vanderhye

[57] **ABSTRACT**

A compound of formula



wherein Z is a tetrahydro-pyrano group selected from



having antifungal activity processes for their preparation and their use in medicines.

15 Claims, No Drawings

US-PAT-NO: 5854280

DOCUMENT-IDENTIFIER: US 5854280 A

TITLE: Antifungal sordaridin derivatives

----- KWIC -----

NCIMB 40675 is an aerobic, Gram-positive, non-motile irregular rod that produces lemon yellow, translucent, round, entire, convex colonies with a diameter of between 0.5-1 mm when grown on tryptic soy agar supplemented with 2% (w/v) yeast extract for 48 hours at 28.degree. C. The organism grows well at temperatures up to 37.degree. C., but not at 45.degree. C. Metachromatic granules were not observed and the strain is catalase positive, oxidase negative and does not metabolise glucose fermentatively. The strain can utilise the following sources of carbon: .alpha.-D-glucose, D-fructose, p-hydroxyphenyl-acetic acid, D-mannitol, methylpyruvate, lactamide, D-trehalose and sucrose. The organism can only weakly utilise D-gluconic acid, pyruvic acid and salicin as sole carbon sources. Colony and microscopic morphology resembles that of coryneform bacteria. The genus *Corynebacterium* was excluded on the grounds that the peptidoglycan of NCIMB 40675 contains omithine rather than the meso-isomer of 2,6-diaminopimelic acid or diaminobutyric acid. Also, the organism contains a complex mixture of branch chain fatty acids atypical of *Corynebacterium* species, namely, 12-methyltetradecanoic, 14-methylhexadecanoic and 14-methylpentadecanoic acids. The presence of .alpha.-branched-.beta.-hydroxylated fatty acids was not determined. On the basis of these results NCIMB 40675 most closely resembles

one of the following
actinobacterial genera: Aureobacterium, Curtobacterium or
Cellulomonas.